

## **The Ethics of Synthetic Biology: Suggestions for a Comprehensive Approach**

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### **I. Risks and Benefits**

A. The Commission should assess the full range of potential benefits of synthetic biology.

1. Applications include (*inter alia*) renewable biofuels, pharmaceuticals, technical materials, nuclear waste disposal, chemical detoxification, superefficient agriculture, energy harvesting and conversion, and geoengineering. Creating a so-called ‘minimal microbe’ template could streamline the design of biological systems or their components, which could then be engineered for a host of specialized applications, such as those described above.

2. In addition, the capacity to engineer and reverse-engineer organisms may vastly increase our knowledge of the complex causal relations between genomes and the functional properties of living things, leading to unanticipated benefits.

B. The Commission should determine which of the identified benefits can only be obtained, or obtained at reasonable cost, through synthetic biology. It should evaluate what if any advantages synthetic biology has over alternative emerging technologies, such as genetic modification, the manipulation of gene expression through the alteration of transgenerationally and somatically heritable epigenetic effects, and nanotechnology, as well as more traditional forms of medicine. Understanding the comparative advantage of synthetic biology will be crucial for making risk/benefit assessments, especially if it should turn out that synthetic biology poses distinctive risks.

C. The Commission should recognize that the realm of synthetic biology is broad, and includes not only the creation of new complete organisms but also living components that do not rise to the level of life forms, let alone complex life forms. It is unlikely, therefore, that any single, all-encompassing approach to risk management will be able to accommodate the diversity of risk issues that are likely to arise in connection with synthetic biology. As a result, the Commission should consider whether different regulatory approaches are appropriate for different areas of the domain.

D. The Commission should develop a comprehensive classification of the risks of synthetic biology and attempt to determine which risks, if any, are peculiar to this technology.

E. In our view, the most important classes of risks in the context of synthetic biology are (1) the risk of unintended consequences, and (2) the risk associated with “dual use.” We believe that both are serious, but that the dual use risk may be the most difficult to address and should therefore be a primary focus of the Commission’s deliberations. Below we first note that there are in fact two distinct Dual Use problems. We then identify and discuss three major concerns regarding unintended consequences, in descending order of their perceived significance. These include

harm to health and the environment, versions of the “playing God” worry that are framed in terms of the limitations of human knowledge, and the devaluing of life.

## **II. Dual Use**

A. It is important that the Commission note that there are in fact two kinds of dual use problems. The first (Dual Use 1) is the worry that dangerous synthetic organisms or the recipes to cook them up could fall into the hands of non-state actors bent on acts of terror, or the authoritarian rulers of “rogue states.” The second dual use problem (Dual Use 2) is the concern that the knowledge output of synthetic biological research and development could be incorporated into the offensive bioweapons programs of developed states. The Commission should therefore recognize that measures designed to reduce the risk of Dual Use 1 cases can, under certain circumstances, exacerbate the risks of Dual Use 2. For example, a government-funded anti-bioterrorist initiative may stimulate research that the government then uses for offensive purposes. Notoriously, the line between defensive and offensive bioweapons development is hard to draw and accountability for keeping within the limits of defense is difficult. In addition, grants for anti-bioterrorism research will result in more people being trained in skills that could be used for terrorist purposes.

B. As the 1996 report of the President’s Advisory Committee on Human Radiation Experiments reveals, there are serious risks associated with complicity between leading figures in science and unethical government programs carried out with elements of secrecy and in times of perceived national emergency. The Advisory Committee reviewed radiation research that was sponsored by the federal government between 1944 and 1974. These experiments were conducted in furtherance of biomedical knowledge and national defense, and were routinely carried out without consent of or benefit to the human subjects involved. The Commission should therefore pay careful attention to the ethical dimensions of the relationship between scientists and those in charge of national defense.

C. At present it is unclear whether it is reasonably possible for state or non-state actors to design pathogens that could be significantly more harmful than wild types. Hence, the Commission might request that more research be done to determine whether this is possible and, if so, what implication it might have for dual use dilemmas. Note that assessing the potential potency of synthetic biological agents could itself carry dual-use related risks.

## **III. Harm to Health, Ecosystems, and the Environment**

A. The Commission should avoid invoking or tacitly appealing to simplistic notions of the ‘benevolent balance of nature’ that have little theoretical or empirical grounding in contemporary evolutionary and ecological science. The problem is that such metaphors may distort a rational calculation of risks and benefits. [For an elaboration of this theme, see R. Powell and A. Buchanan, “Breaking Evolution’s Chains: The Prospect of Deliberate Genetic Modification in Humans,” *Journal of Medicine and Philosophy*, forthcoming].

The Commission should ensure that its assessment of the risks of synthetic biology is not distorted by fallacious views of nature and the natural, and that its judgments are informed by the best available evolutionary and ecological science. In particular, the Commission should avoid giving credence to objections to synthetic biology that are based on pre-Darwinian or teleological views of nature. It should not view “natural” organisms as akin to the products of a master

engineer. Instead, it should acknowledge the severe engineering constraints and human costs involved in unassisted evolutionary processes, and the ways in which emerging biotechnologies, including synthetic biology, might overcome some of these constraints and reduce some of these costs.

More generally, the Commission should avoid giving credence to uses of terms such as ‘normal’, ‘natural’, ‘nature’, and ‘human nature’ that disguise controversial moral assumptions as descriptive, factual claims. [For examples of this error, see President Bush’s Council on Bioethics, *Beyond Therapy*].

B. While the release of synthetic or genetically engineered organisms into the wild remains a concern, there is to date little evidence that the deployment of GMOs has resulted in major ecosystem disruption or collapse, as many had feared. Nor have any serious negative health effects from the ingestion of genetically modified foods been demonstrated. Thus, the Commission should ask the following questions: Is there any reason to think that the products of synthetic biology pose inherently different levels or qualities of risk to health, ecosystems and the environment than their genetically modified counterparts? How would fabricated organisms of varying biochemical and genetic constitutions interact with living systems and ecosystems?

C. Here, it might be helpful to consult the astrobiological literature concerning the risks associated with extraterrestrial back-contamination in the context of NASA sample-return missions, which presumably has considered the ecological implications of introducing life forms of radically different biochemical makeup. The Commission should recognize, however, that there is much controversy surrounding the ecological impact of introduced organisms. There seem to be two schools of thought on this matter. The first holds that the risk of negative interaction between introduced (e.g. synthetic) and endemic (e.g. non-synthetic) lineages would be minimal. It reasons that the extent of interaction between the lineages would be limited, given that strategic co-evolution requires prolonged evolutionary contact, and that in any case species will tend to diverge so as to avoid direct competition. The second school of thought holds that endemic organisms and ecosystems are at high risk of being ravaged by invaders, since they are essentially akin to ‘naïve’ prey or competitors that are not adapted to defend and compete against these alien intruders. A more thorough understanding of the relevant causal, evolutionary and ecological variables is required in order to resolve these questions to any degree certainty.

D. The Commission should weigh potential harms to ecosystems against the potential benefits that synthetic life technology may have for repairing damage to such systems (see I.A.1 above).

E. Another common environmental concern in the context of GMOs is the so-called “pollution” or “contamination” of gene pools. This worry could be extended to synthetic life sciences if there is a possibility that synthetic organisms could exchange genes with wild types (e.g. via lateral gene transfer if they are sufficiently similar genomically). This would be a legitimate worry if there was evidence that such events (were they to occur) would have ecologically harmful consequences. In the absence of such evidence, “genetic pollution” should not be a major concern for the Commission, since in our judgment views about the supposed value of “genetic purity” tend to rely on problematic conceptual and normative assumptions about “the natural” that the Commission would do well to avoid. [For an elaboration of this point, see A. Buchanan, “Enhancement and Human Nature,” *Bioethics* 23(3): 141-150, 2009].

G. The Commission should look to ways of reducing health and environmental risk by drawing on strategies of containment and reversibility that were developed in the context of genetic modification technologies. One example of a containment strategy is the design of synthetic

organisms with a crucial auxotrophy, that is, the inability to synthesize some organic compound necessary for its life cycle.

H. The Commission should make it clear that dual use problems and the risks of unintended harms are *ethical* issues, not merely scientific, political, or policy issues, as some bioethicists have suggested. There is a crucial role for moral and political philosophy in identifying what count as harms and benefits, in weighing harms and benefits, and in balancing the conflicting rights and interests of various stakeholders all of whom may have legitimate moral claims. Any recommendations the Commission makes regarding the formation or continued operation of oversight or consultative bodies should include provision for input from persons trained in ethics.

I. The Commission should be clear that in focusing on unintended consequences, it is not adopting or otherwise endorsing consequentialism. The harms that are envisioned are harms to persons, and they are morally undesirable on virtually any plausible philosophical account of morality, whether consequentialist or otherwise.

J. The Commission should make it clear that the goal is not to eliminate risk, but to limit it to acceptable levels. Elimination of risk is rarely attainable and beyond a certain point additional risk reduction is likely to be too costly. In terms of institutional design, this means recognizing that different actors may have different incentives that encourage them to either overestimate or underestimate the costs of risk-reduction.

K. The Commission should help develop cautionary heuristics for synthetic biology that are knowledge-sensitive, that encourage relevant knowledge-acquisition, and that take into account the potentially significant benefits of weaker restrictions. The Commission should be wary of reliance on a single risk-reduction or prevention principle, such as the Precautionary Principle, and recognize that reliance on a plurality of risk-reduction heuristics, to be modulated over time in the light of increasing knowledge, is much more reasonable.

#### **IV. Other Ethical Concerns**

##### **A. “Playing God.”**

1. A common criticism of emerging biotechnologies takes the form of an admonition that scientists should not “play God.” The “playing God” objection is a familiar one in the context of genetic modification, and it is likely to be advanced even more vigorously against synthetic biology, which represents perhaps the paradigmatic case of playing God insofar as it enables us to design and create life “de novo” (an ability often imputed to God), as opposed to simply modifying living structures (but see IV.B.3.a below on the fuzzy boundary between modification and synthesis).

There are several ways to construe this criticism. One is metaphysical or theological, asserting that humans should not intervene in certain realms of the natural world regardless of what the likely consequences of such interventions will be. Some people believe that the genetic modification or de novo creation of living organisms encroaches into such a forbidden realm, and hence they believe that there is something intrinsically wrong with these activities, which warrants their prohibition. While we recognize that many people may share these intuitions, we do not think that they justify placing an all-things-considered moratorium on synthetic life technology and foregoing the potentially enormous benefits that it might produce.

2. Another way to construe the playing God objection is in terms of moral character: the idea here is that the development and deployment of genetic engineering and synthetic life technology reflects a hubristic desire for total mastery over nature. We believe that this criticism is unfair in that it attempts to discredit the motivations of all of those who promote emerging biotechnology, many of whom are motivated not by a desire to master nature but by the prospective social benefits of these technologies. Like attempts to enhance human capacities by biomedical means, the use of synthetic biology need not signal a desire for perfection or total mastery, but only a reasonable commitment to improving human life.

3. Because intervention in nature in furtherance of human good is widely accepted in religious and secular circles alike (consider the eradication and treatment of disease, for example), one would need to come up with a principled basis by which to distinguish hubristic interventions that amount to playing God from those that are laudably foresighted, realistic, and desirable. The focus, therefore, should be on the identification of risks, including the “meta-risk” that we will overestimate our ability to act without undue risk. It is important to emphasize that the mere identification of this risk is not an objection to synthetic biology. The question is how serious this risk is compared to the benefits and whether there are morally acceptable means of reducing the risk to reasonable proportions.

4. More plausible is the epistemic version of the “playing God” objection, which expresses the concern that we might fail to admit the limitations of our knowledge in tinkering with complex systems. However, we believe that even this version of the “playing God” objection should not be a substantial focus of the Commission. The epistemic version of the “playing God” objection is not helpful because it is not evidence-sensitive, does not encourage the acquisition of relevant knowledge regarding the causal structure of the biological systems in question, offers no substantive guidance with respect to the development of more appropriate safeguards based on that knowledge, and fails to take into account the potentially significant benefits of the technology.

5. As in the case of genetic modification, the Commission should not assume that there is anything *inherently* ethically problematic about altering or synthesizing living systems, apart from the harmful consequences they may have, including their effects on human relationships, attitudes, and values.

## B. Humankind’s Relationship to Nature

1. Another worry, expressed also in the context of genetic modification, is that the design and manufacture of life will blur the artifact (or machine)/organism distinction, leading to the devaluing of life, or encouraging the belief that all life is of merely instrumental value.

a. The Commission should not assume that the distinction between organisms and artifacts, or between machines and living things, as might be applicable in the context of synthetic biology, is itself morally significant. Instead, it should stress that what matters for the purposes of ethical analysis is the existence of morally relevant properties, and that morally relevant properties are generally functional properties (such as homeostasis, sentience, consciousness, or personhood) that do not require any particular biochemical makeup or historical etiology. Generally speaking, how a being came to exist is not relevant to its moral status. For example, a person is a person, with all the rights this entails, regardless of whether she came to be through ordinary sexual reproduction, IVF, or, for that matter, cloning. The Commission should therefore not assume that the distinction between creating life via synthetic biology and creating it through other

technologies, such as genetic engineering, embryo selection, sperm sorting, or IVF, is morally significant in itself, much less that it has implications for moral status.

2. Some bioethicists have expressed the view that synthetic biology is the ultimate victory of reductionism, since it shows that life is “just a conglomeration of molecules” and therefore not “sacred.” We think that this interpretation of work in synthetic biology is both metaphysically and normatively misguided. First, synthetic biology does not demonstrate that higher-level properties ‘reduce’ to lower level properties any more than work in ordinary molecular-development shows this to be the case. Second, even if it is true that higher-level properties (such as homeostasis or sentience or consciousness) reduce to lower-level properties, this has no implication whatsoever for moral status. Moral status depends on the existence of certain higher-level properties regardless of whether they reduce (or are irreducible) to lower-level ones. So far, ethical discussions of the supposed reductionism of synthetic biology [e.g. Cho et al., “Ethical considerations in synthesizing a minimal genome,” *Science* 286(5447): 2087-2089, 1999] have been based on the conflation of different senses of ‘reductionism’ and mistaken assumptions about the implications of reductionism for the moral status of living things and the relationship between human beings and nature. The Commission could make an important contribution by providing a careful analysis of the relationship between reductionism and synthetic biology, and the ethical implications of this relationship.

a. The Commission should stress that although the question of what constitutes a living thing is philosophically interesting, the resolution of this debate has no bearing on the analysis of risk or other substantive ethical issues associated with synthetic biology.

3. In determining whether there are any unique ethical issues that arise in the context of synthetic biology, the Commission should recognize that the conceptual boundary between genetic modification and synthetic biology is unclear.

a. On one end of the synthesis/modification continuum, genomes are assembled from inorganic molecules and then translated into living organisms (or functional components) without the aid of non-synthetic organic materials. In another case, viral-sized snippets of DNA generated by non-synthetic living systems are arranged to produce an unprecedented organism (or functional component), with or without the aid of other non-synthetic living systems. As we move toward the genetic modification end of the spectrum, we encounter radical, moderate, and minimal modifications to the genomes of existing organisms or their expression patterns. Note also that purely synthetic biological components may play an increasingly important role in the genetic modification of existing organisms.

b. Even if there is a defensible distinction between the synthesis and modification of biological entities, we do not see any *ethical* reason for attempting to formulate a bright line between these overlapping technologies.

4. With regard to the anticipated public response to synthetic biology, the Commission should avoid a priori predictions about social attitudes toward developments of this technology, and it should realize that initial attitudes are likely to change as the technology becomes more commonplace. (Recall the welter of false a priori predictions about the social stigma that persons created through IVF would suffer). For the same reason, the Commission should avoid armchair predictions about the social effects of predicted attitudes, e.g., that people will lose their “reverence” or “respect” for life if we were able to (and did) create it. These are empirical questions, and even if these predictions are to some degree borne out, it remains an open policy

question whether the negative effects of social attitudes and prejudices are better addressed through public education programs rather than through the prohibition of synthetic life technology.

5. The Commission should consider both the “playing God” admonition, and the worry that synthetic biology could lead to the devaluing of life, not as conclusive objections to the development and use of synthetic life technology, but rather as concerns that must be balanced against the latter’s potentially significant benefits.

## **V. Justice**

A. The Commission should make considerations of justice a central focus of its inquiry concerning synthetic biology. It should ask, for instance, what are the implications of synthetic biological innovations for human wellbeing and the environment in developed and developing nations, respectively? One concern, which applies equally to conventional pharmaceuticals, is the lack of financial incentives for pharmaceutical companies to design and manufacture synthetic biological agents for predominantly poorer markets where they are most needed.

1. In exploring justice-related issues, the Commission should consider whether the current intellectual property rights regime is equipped to accommodate synthetic life technologies, including the synthesis of many genes in combination to form a single functional organism. The Commission should make it clear that intellectual property regimes can serve multiple goals and that viewing them simply as mechanisms for the “maximization of innovation” is simplistic. The distributive effects of intellectual property regimes, as well as their effects on innovation, ought to be considered.

2. In its consideration of justice issues, the Commission should avoid “synthetic biology exceptionalism,” and instead regard this technology as one instance of the larger phenomenon of innovation. [See A. Buchanan, A. Cole, and R.O. Keohane, “Justice in Innovation,” *Journal of Political Philosophy*, 2011 (available online at Early View, Wiley-Blackwell Publishers)].

## **VI. Public Policy and Institutional Design**

A. The Commission should remember that ethics needs help from incentives. It should therefore be critical about proposals that rely primarily on voluntary constraints by scientists in response (for instance) to dual use concerns. The Commission should carefully consider the institutional effects of any policy recommendations, and also seek to determine what institutional innovations may be needed, taking into account sound principles of institutional design.

1. To this end, the Commission should consider whether and to what extent a division of moral labor is preferable—that is to say, whether the public interest is better served by encouraging individual scientists mainly to focus on the acquisition of knowledge while tasking government, independent regulatory bodies, and professional organizations with the ultimate responsibility for ethical oversight of such activities.

2. The Commission should think in terms of designing institutions that are primarily tasked with the acquisition and dissemination of knowledge, but it should recognize that there are a number of goals and interests at stake. It should therefore aim for *optimization*, rather than the maximization of knowledge acquisition or risk reduction. For example, it is a mistake to think

that in coping with the risk of Dual Use 1 (see II.A above) there are only two values to be balanced: namely, scientific freedom and security. A number of other factors must be taken into account as well, including the prospect that anti-bioterrorism initiatives will result in the unacceptable growth of government power or in unjustifiably relaxed standards for the treatment of human or animal subjects in research (see II.B above).

3. The Commission should consider problems of international governance that might arise in connection with synthetic bioweapons programs that are developed either by states or non-state actors, and which might pose a serious global risk. For instance, it should anticipate the practical and legal difficulties that are likely to be encountered in attempting to prevent the proliferation of dangerous synthetic biological agents and technologies, which may be even more difficult to contain and track than nuclear weapons materials. Moreover, it should consider whether existing regulations and governmental resources are sufficient to guard against the risks associated with the proliferation of cheap genome synthesis technology and the availability of dangerous sequence information.